















Claim 88 (Previously presented): The method according to claim 86, wherein the Type II collagen degradation results in a loss of proteoglycan, cleavage of type II collagen into a TCA degradation product, a change in joint function, joint space narrowing, destruction of cartilage, a change in growth plate morphology, fibrillation and loss of articular cartilage, osteophyte formation, or combinations thereof.

Claim 89 (Previously presented): The method according to claim 87, wherein the Type II collagen degradation results in a loss of proteoglycan, cleavage of type II collagen into a TCA degradation product, a change in joint function, joint space narrowing, destruction of cartilage, a change in growth plate morphology, fibrillation and loss of articular cartilage, osteophyte formation, or combinations thereof.

Claim 90 (Currently Amended): A method for evaluating the potential of a composition to counteract degradation of Type II collagen in joints of a transgenic non-human mammal, which degradation results in a ~~phenotypic change~~ phenotype selected from the group consisting of loss of proteoglycan, cleavage of Type II collagen into a TCA degradation product, a change in joint function, joint space narrowing, destruction of cartilage, a change in growth plate morphology, fibrillation and loss of articular cartilage, osteophyte formation, and combinations thereof, which method comprises:

(a) providing a first and second transgenic non-human mammal of claim 55;

(b) ~~in which a phenotypic change has been produced by activation of~~ activating expression of the metalloproteinase at the same age during adulthood of the transgenic non-human mammals, wherein expression of the metalloproteinase results in a phenotype selected from the group consisting of loss of proteoglycan, cleavage of Type II collagen into a TCA degradation product, a change in joint function, joint space narrowing, destruction of cartilage, a change in growth plate morphology, fibrillation and loss of articular cartilage, osteophyte formation, and combinations thereof;

~~(b)~~ (c) administering the composition to the first transgenic non-human mammal; and

~~(e)~~ (d) comparing the phenotype of the first transgenic non-human mammal to which the composition was administered with the phenotype of the second transgenic non-human mammal in which the composition was not administered,

wherein any less extensive development in the nature or extent of the ~~phenotypic change~~ phenotype in the first transgenic non-human mammal or any increased length of time required for the ~~phenotypic change~~ phenotype to develop in the first transgenic non-human mammal that has been administered the composition relative to the ~~phenotypic change~~ phenotype in the second transgenic non-human mammal, indicates the potential of the composition to counteract the ~~phenotypic change~~ phenotype resulting from degradation of the Type II collagen in joints of a transgenic non-human mammal.

Claim 91 (Currently Amended): A method for evaluating the potential of a composition to counteract degradation of Type II collagen in joints of a transgenic non-human mammal, which degradation results in a ~~phenotypic change~~ phenotype selected from the group consisting of loss of proteoglycan, cleavage of Type II collagen into a TCA degradation product, a change in joint function, joint space narrowing, destruction of cartilage, a change in growth plate morphology, fibrillation and loss of articular cartilage, osteophyte formation, and combinations thereof, which method comprises:

(a) providing a first and second transgenic non-human mammal of claim 60;

(b) ~~in which a phenotypic change has been produced by activation of~~ activating expression of the metalloproteinase at the same age during adulthood of the transgenic non-human mammals, wherein expression of the metalloproteinase results in a phenotype selected from the group consisting of loss of proteoglycan, cleavage of Type II collagen into a TCA degradation product, a change in joint function, joint space narrowing, destruction of cartilage, a change in growth plate morphology, fibrillation and loss of articular cartilage, osteophyte formation, and combinations thereof;



(e) (d) comparing the phenotype of the first transgenic rat to which the composition was administered with the phenotype of the second transgenic rat in which the composition was not administered,

wherein any less extensive development in the nature or extent of the ~~phenotypic change~~ phenotype in the first transgenic rat or any increased length of time required for the ~~phenotypic change~~ phenotype to develop in the first transgenic rat that has been administered the composition relative to the ~~phenotypic change~~ phenotype in the second transgenic rat, indicates the potential of the composition to counteract the ~~phenotypic change~~ phenotype resulting from degradation of the Type II collagen in joints of a transgenic rat.

Claim 93 (Currently Amended): A method for evaluating the potential of a composition to counteract degradation of Type II collagen in joints of a transgenic non-human mammal, which degradation results in a ~~phenotypic change~~ phenotype selected from the group consisting of loss of proteoglycan, cleavage of Type II collagen into a TCA degradation product, a change in joint function, joint space narrowing, destruction of cartilage, a change in growth plate morphology, fibrillation and loss of articular cartilage, osteophyte formation, and combinations thereof, which method comprises:

(a) providing a first and second transgenic non-human mammal of claim 75;

(b) ~~in which a phenotypic change has been produced by activation of~~ activating expression of the metalloproteinase at the same age during adulthood of the transgenic non-human mammals, wherein expression of the metalloproteinase results in a phenotype selected from the group consisting of loss of proteoglycan, cleavage of Type II collagen into a TCA degradation product, a change in joint function, joint space narrowing, destruction of cartilage, a change in growth plate morphology, fibrillation and loss of articular cartilage, osteophyte formation, and combinations thereof;

(b) (c) administering the composition to the first transgenic non-human mammal; and







